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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/030,787 | 01/31/2002 | Nikos Pagratis | NEX87/PCT-US | 6400 |
| 25871 | 7590 | 08/26/2005 | EXAMINER | |
| SWANSON & BRATSCHUN L.L.C. 1745 SHEA CENTER DRIVE SUITE 330 HIGHLANDS RANCH, CO 80129 | | | FORMAN, BETTY J | |
| | | | ART UNIT | PAPER NUMBER |
| | | | 1634 | |

DATE MAILED: 08/26/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/030,787

Applicant(s)

PAGRATIS ET AL.

Examiner

BJ Forman

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 31 May 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 2-7 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 2-7 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

DETAILED ACTION

1. Applicant's request for reconsideration of the rejections in the last Office action is persuasive and, therefore, the finality of that action is withdrawn.

Status of the Claims

2. This action is in response to Appeal Brief filed 31 May 2005 in which the previous rejections under 35 U.S.C. 112, first paragraph were traversed. Applicant's arguments have been thoroughly reviewed and found persuasive.

The previous rejections in the Office Action dated 7 December 2004 under 35 U.S.C. 112, first paragraph are withdrawn in view of the arguments.

New grounds for rejection are discussed.

Claims 2-7 are under prosecution.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite for the recitation "Linker between said ligand and said or lipophilic compound" because it is unclear why "Linker" is capitalized. The recitation is further indefinite because it is unclear whether "or" is incorrectly inserted into the recitation or whether words are missing before and/or after the word "or".

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

6. Claims 2-7 are rejected under 35 U.S.C. 103(a) as obvious over Toothman et al (U.S. Patent No. 5,731,424 issued 24 March 1998) in view of Parma et al (U.S. Patent No. 5,766,853, issued 16 June 1998).

The claims are drawn complexes comprising a TGF β 2 nucleic acid ligand and non-immunogenic or lipophilic compound wherein the complex further comprises a linker and wherein the compound is PEG having a molecular weight of 10-80 or 20-45K.

Toothman teaches complexes comprising TGF β nucleic acid ligands wherein the ligands include TGF β 2 nucleic acid ligands (Column 5, lines 13-19) and wherein the ligands are complexed with compounds to increase *in vivo* stability of the ligand (Column 8, lines 23-36) as known in the art as "post-SELEX" modification. Toothman et al does not teach the claimed PEG modification. However, Parma teaches the "post-SELEX" modification as suggested by Toothman et al. Parma et al specifically teach post-SELEX modifications to increase *in vivo* stability of the ligand (Column 11, line 59-Column 12, line 17) wherein the modification includes PEG of about 80K (Example 1, Column 14, lines 1-4). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the PEG modification to the TGF β 2 nucleic acid ligands of Toothman. One of ordinary skill in the art would have been motivated to do so based on Toothman's expressed teaching to do so (Column 8, lines 23-36). One of ordinary skill would have been further motivated with a reasonable expectation of success based on the working example of Parma and for the expected benefit of

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increased *in vivo* stability of the ligand as desired by Toothman (Column 11, line 59-Column 12, line 17) and Parma (Column 11, line 59-Column 12, line 17).

Double Patenting

7. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

8. Claims 2-7 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Patent No. 5,731,424 in view of Parma et al (U.S. Patent No. 5,766,853, issued 16 June 1998).

Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to complexes comprising a TGF β nucleic acid ligands and differ in that the instant claims define the ligands as complexes comprising a TGF β 2 nucleic acid ligand. However, the '424 disclosure defines the patent ligands as complexes comprising a TGF β 2 (page 5, lines 16-19). Therefore, the patent ligand encompasses the scope of the instantly claimed ligands. The claims further differ in that the instant claims define the compound linked to the ligand as a high-molecular weight or lipophilic compound (e.g. PEG). The '424 disclosure defines the preferred embodiment of the ligand complex including a modification to increase *in vivo* stability of the ligand (Column 8, lines 23-36) as known in the art as "post-SELEX" modification.

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Parma teaches the "post-SELEX" modification as taught in the '424 disclosure. And Parma et al specifically teach post-SELEX modifications to increase *in vivo* stability of the ligand (Column 11, line 59-Column 12, line 17) wherein the modification includes PEG of about 80K (Example 1, Column 14, lines 1-4). It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to apply the PEG modification to the patent. One of ordinary skill in the art would have been motivated to do so based on the '424 disclosure's expressed teaching to do so (Column 8, lines 23-36). One of ordinary skill would have been further motivated with a reasonable expectation of success based on the working example of Parma and for the expected benefit of increased *in vivo* stability of the ligand as desired in the '424 patent (Column 11, line 59-Column 12, line 17) and Parma (Column 11, line 59-Column 12, line 17).

Conclusion

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (571) 272-0745. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

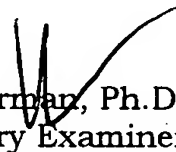
Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions


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daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.



BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
August 22, 2005



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